chemistry texts for them and for the vast amount of time and thought they have spent in the preparation thereof. I often wonder, however, if the college teacher who lives and works among college students and does some research on the side can be expected to guage the needs of the secondary student and to put himself in the place of the secondary school teacher. If such a college man could have an opportunity to fill the position of a secondary school teacher of chemistry for a period of say five years, and have to make his living thereby, I'd welcome a text he might produce. Or must we wait till the profession of chemistry teaching in secondary schools has become sufficiently established to attract men of the requisite scholarship, knowledge of chemistry, acquaintance with what the colleges should require for entrance, and above all a close knowledge of the mental equipment of students of secondary school age before we can expect a solution of the problem: "What should be taught in first year chemistry and how should it be presented?"

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THE PHYSICO-CHEMICAL MECHANISM OF MUTATION AND EVOLUTION

IT is the general rule in biology that descendants resemble parents, and that a parent organism can not pass on to offspring a factor which the parent did not receive from the germ-plasm of its immediate progenitors. Many apparent exceptions to this general rule have been traced to the existence in the parent gametes of recessive factors, which, while suppressed in the parent, may be liberated again in the offspring. Whether we accept the view of Darwin that large differences can represent the summation of small differences, or the more probable view of Bateson and others, that mutation or variation is a definite physiological event, no satisfactory explanation has been given as to the origin or source of these exceptions to the general rule of resemblance, although they constitute the steps by which evolution haltingly proceeds.

The crying need that we must find a chemical, physical or physico-chemical basis for mutation or variation has been voiced by many. Thus in his address before the British Association for the Advancement of Science (Australia, 1914, reprinted in *Smithsonian Report,* 1915, pp. 359-394), Sir William Bateson says: "Every theory of evolution must be such as to accord with the facts of physics and chemistry, a primary necessity to which our predecessors paid small heed. . . . Of the physics and chemistry of life we know next to nothing. Somehow the characters of living things are bound up in properties of colloids, and are largely determined by the chemical powers of enzymes, but the study of these classes of matter has only just begun. Living things are found by simple experiment to have powers undreamt of, and who knows what may be behind?"

Recently R. S. Lillie[1] (SCIENCE, 51, 525, 1920) has stressed the importance of physico-chemical investigation of protoplasm, and Alexander Forbes (SCIENCE, 52, 331, 1920) has called for closer cooperation between physicists and biologists in attacking biological problems.

An attempt will be made here to outline certain basic physico-chemical principles which affect the formation, development, growth and reproduction of living things, and to point out how it is possible for variation in some of the factors therein involved to account for important and transmissible variations or mutations in individual organisms.

At the outset let it be stated that no mysterious or special "vital force" will be evoked, but that the well-known forces that control inanimate matter seem quite sufficient for the purpose.

In nature, both animate and inanimate, the following basic factors tend to produce *symmetrical orientation or aggregation:* (1) Crystallization; (2) Diffusion, as in the formation of Liesegang's rings, agate, etc.; (3) Electric or magnetic fields of force; (4) Harmonious vibration as of air, water, etc. We here disregard mere chance and the conscious arrangement by man.

[1] See also Lillie's interesting papers in *Biological Bulletin,* 1917-1919, and *Scientific Monthly,* February, 1922.

The main factors modifying the crystallization of pure substances are: (1) Concentration; (2) Temperature; (3) Pressure; (4) Agitation; (5) The presence of other substances, especially of colloids, which may profoundly modify crystal forms by protective action; (6) Iso-colloidism. Some substances have the power of interfering with their own crystallization, because a portion, which first reaches the colloidal state, then protects the balance.

Deviations from normal crystalline forms produced by the presence of colloids are usually symmetrical, but may not appear crystalline. Changes in the nature or degree of dispersion of the colloid, or in its percentage, mixtures of colloids, variations in salt or H-ion concentration of the solution, must all have an effect on the resultant quasi-crystals. Enzymes may, of course, entirely change the nature of the colloid. The species-specificity of proteins seems to be maintained by degenerating food protein to simpler forms (polypeptids and amino-acids) and then building up the specific proteins from these.

Among the factors influencing diffusion, especially in gels, are the chemical nature and particle size of the gel, and the concentration and nature of the diffusing solution. Liesegang has pointed out that "enzoon," which has been considered to be the fossilized remains of primitive organisms, is due to the phenomenon that bears his name—the rhythmic banding resulting from diffusion in gels. In his chapter on "Growth, Metamorphoses and Development" Bechhold ("Colloids in Biology and Medicine," trans. by J. G. M. Bullowa, p. 252 *et seq.,* D. Van Nostrand Co., 1920) refers to some of the remarkable diffusion figures and osmotic forms produced by F. E. Runge and by Stéphane Leduc, some of which resemble algæ, fungi, seaweed, etc., and even show a cellular microstructure. While pointing out the great differences between these formations and the organized structures they simulate, Bechhold says: "The physical forces which produced these inorganic formations are the same as those which produce the growth and configuration of organized material membranes, osmotic pressure, diffusion."

Differences in diffusion speed mean variations in concentration that may affect the action of the enzymes, for, as T. B. Robertson showed, these may work analytically or synthetically, depending on the concentration.

A preliminary note of this character can not consider all of the points above referred to, and will therefore be limited mainly to a brief discussion of one of the most important factors controlling the form of organisms, namely, *the influence of colloids on crystallization,* and the changes in form that may be expected when the colloids are changed or the crystalizing substances varied.

Perhaps the most familiar instance of modified crystallization is to be found in the delicate frost tracery on window panes, the forms being probably influenced by the glass (itself a colloid) or by substances adsorbed at its surface. The writer has pointed out the powerful influence exerted by colloids such as gelatin, gum arabic and albumin on crystallization (*Kolloid Zeit.,* 4, 86, 1909), and R. E. Liesegang, looking at the question from the opposite standpoint, has described the power of crystalloids to give a form to colloidal jellies (*Kolloid Zeit.,* 7, 96, 1910). It may be said that with different salts or combinations of salts, various colloids or combinations of colloids, and variations in concentrations, temperature and speed of evaporation, will produce characteristic and generally reproducible forms on a microscope slide. A characteristic form of sodium chloride is a four pointed star with fern-like arms which cross at a slight angle.

A few slides made with solutions of common salts such as $NaCl$, $MgSO_4$, Na_2SO_4, etc., containing from 0.5 to 50 per cent. of gum arabic or gelatin (figured on the basis of the dry salt) will illustrate what is meant. When a drop of the mixed solution is allowed to dry on the slide without cover glass, changes of concentration and temperature occur, giving a field that changes progressively from rim to center of the drop. A solution of one part sodium chloride, one part sodium carbonate (dry) and one tenth part gum arabic or gelatin in ten parts of water, when dried, shows in some part of the field a "flowering plant," with graceful stems and characteristic four-petaled flowers.

To see that a marked change may be produced by modifying the colloidal state of the protective substance, a slide was made with a solution containing egg albumen as the colloid. The solution was then heated until the albumen began to show a milkiness, another slide was made, and after drying was compared with the first unheated specimen. The difference in crystallization is considerable.

Unusual crystalline forms such as sphero-crystals and sheaf-like groups which are so often seen in the crystals of substances derived from organisms, are very often consequent upon the protective action of some colloid from which they are not entirely purified. Another curious occurrence must be mentioned here, which may be termed *auto-protection* because it is due to iso-colloidism. Before reaching the ordinary visibly crystalline state, particles of every substance must pass through the colloidal zone, and the particles first reaching that state may interfere with the normal crystallization of the rest. Thus ammonium salts, even without the addition of protective colloids, are prone to assume feathery or fern-like forms. The phenomenon is marked in the oleates and is probably the underlying cause of the formation of myelins, although their formation is fostered by such lipoid protectors as cholestrin. According to J. G. Adami (Harvey Society Lecture, 1906), if certain simple soaps be dissolved by warming on a slide with water and then allowed to cool, they may show upon examination in the polarizing microscope a perfect rain of doubly refracting spherules, which, depending on the nature of the soap, may last for hours or days or else immediately give place to a brilliant white layer of formed crystalline plates. The fluid crystals of O. Lehmann are probably examples of auto-protection, and W. B. Hardy, E. Hatschek and others have described substances which form unstable gels that soon become crystalline.

An indication that the colloidal state is anomalous is given by the fact that, while the sun attracts microscopic particles, and even crystalloidally dispersed particles, it selectively repels colloidally dispersed particles, as in the tails of comets (See J. Alexander, "Colloid Chemistry").

The bio-colloids are so readily affected by salts, H-ion concentration (effective reaction), temperature, actinic (sun's rays) and traumatic (shaking, mechanical injury) effects, that it is more surprising that plants and animals should breed true, than that they should show variations. Therefore, although individuals may be much affected by such changes during their lives, it is evidently a rare occurrence that these changes are registered in the germ plasm by which alone they may be transmitted to offspring. The specificity of the germ plasm is evidently guarded by many factors, among which seem to be selective adsorption and differential diffusion of dissolved substances through its protecting walls or membranes. Nevertheless unusual influences must occasionally change it materially without destroying it, and along this line experiment may be directed. It may be that the germ plasm can be affected through the somatoplasm, as well as by direct means. And of all the variations, in nature only the beneficial changes survive.

With highly developed organisms the complications are enormous. We are just beginning to realize the importance of enzymes, hormones, internal secretions (endocrines), essential "impurities" like the vitamines, iodine and manganese, and the necessity of a sufficient variety of food to include enough of each of the essential amino-acids, outside of mere fat-carbohydrate-protein-calorie figures. Therefore, even if experiments with higher forms of life may yield more numerous results, it may be better to begin with the simpler forms where the results may be more readily traced to their causes. Nor must it be imagined that this will prove an easy matter; for filterable bacteria, invisible in the ordinary microscope and not resolvable by the ultra-microscope if visible in it, whose size is of the order of some of the protein molecules, are still capable of breeding true.

Consideration should be especially given to conditions that are apt to be met with in nature or which may have existed in geologic times. The effect of small quantities of substances such as manganese in plants and iodine in mammals should not be overlooked. Even strong acidity or alkalinity may be produced

by volcanic action or by differential diffusion in the earth or in unorganized matter. The slime of some snails carries as much as three per cent. of free sulphuric acid. Temperature, light, water and CO_2 are potent factors.

While the actual experimental work is largely the province of biologists, they will gain much both in direction and interpretation by close consultation with the chemists and physicists.

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SCIENTIFIC EVENTS

ANIMAL EXPERIMENTS IN GREAT BRITAIN[1]

THE annual return showing the number and nature of experiments on living animals during the year 1921 gives a list of all "registered places" where such experiments may be performed, the names of all persons who hold licenses during 1921, together with the registered place for which the license was in force and the number and nature of experiments performed. In the year 1921 twenty new places were registered for the performance of experiments and thirteen places were removed from the register. The total number of licensees was 812, of whom 219 performed no experiments. The experiments may be divided into two main groups, according to whether or not an anesthetic was used. It should be noted that the granting of a license only permits the licensee to perform experiments under an anesthetic, for the law declares "the animal must, during the whole of the experiment, be under the influence of some anesthetic of sufficient power to prevent the animal feeling pain; and the animal must, if the pain is likely to continue after the effect of the anesthetic has ceased, or if any serious injury has been inflicted on the animal, be killed before it recovers from the influence of the anesthetic which has been administered." To perform other experiments or even to observe the subsequent course of experiments undertaken with an anesthetic the licensee must be possessed of special certificates. Special certificates are also necessary for experiments on dogs, cats, horses, asses, mules and other large animals. The total number of experiments with anesthetics was 8,165, and of these 2,053 were simple inoculations into the skin of guinea-pigs, which were anesthetized in order to keep the animals motionless during the introduction of a minute quantity of the fluid to be tested for the purpose of standardization. Of the remaining 6,112 experiments, comprising all the cases in which any serious operation was involved, 2,751 were performed under the license alone, and were subject therefore to the restrictions above mentioned. In all operations, with the exception of a few special cases dealing with the efficiency of antiseptics, the law demands that the operation shall be performed antiseptically so that the healing of wounds shall, as far as possible, take place without pain. If the antiseptic precautions fail, and suppuration occurs, the animal must be killed. The following "pain condition" is attached to the license under special certificates: "If an animal, after and by reason of the said experiments, is found to be suffering pain which is either severe or is likely to endure, and if the main result of the experiment has been attained, the animal shall forthwith be painlessly killed. If an animal, after and by reason of the said experiments, is found to be suffering severe pain which is likely to endure, such animal shall forthwith be painlessly killed, whether the main result of the experiment has been attained or not. If any animal appears to an inspector to be suffering considerable pain, and if the inspector directs such animal to be destroyed, it shall forthwith be painlessly killed." The total number of experiments without anesthetics was 67,097. These were mostly simple inoculations and hypodermic injections, but included also some feeding experiments and administration of various substances by the mouth or by inhalation or by external application, and the abstraction of blood by puncture or simple venesection. In no instance was a certificate dispensing with the use of anesthetics allowed for an experiment involving a serious operation. The total number of experiments was 75,262, being 4,895 more than in 1920. The objects for which these experiments were performed were very diverse. A large number, almost wholly simple inoculations, were performed either on behalf of official bodies, with a view to the preservation of the public health or directly for

[1] *The British Medical Journal.*